

substituted heteroaralkyl-; or R_2 and R_2 , taken together form an optionally substituted 3- to 7-membered ring;

[0013] R_{12} is selected from the group consisting of optionally substituted imidazolyl, optionally substituted imidazolyl-, —NHR_4 ; $\text{—N(R}_4\text{)(COR}_3\text{)}$; $\text{—N(R}_4\text{)(SO}_2\text{R}_{3a}\text{)}$; and $\text{—N(R}_4\text{)(CH}_2\text{R}_3\text{)}$;

[0014] R_3 is chosen from hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, optionally substituted heteroaralkyl-, $R_{15}\text{O—}$ and $R_{17}\text{—NH—}$;

[0015] R_{3a} is chosen from optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, optionally substituted heteroaralkyl-, and $R_{17}\text{—NH—}$;

[0016] R_{3b} is chosen from hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, and optionally substituted heteroaralkyl-;

[0017] R_4 is chosen from hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heterocyclyl-, and optionally substituted heteroaralkyl-;

[0018] R_5 , R_6 , R_7 and R_8 are independently chosen from hydrogen, acyl, optionally substituted alkyl-, optionally substituted alkoxy, halogen, hydroxyl, nitro, cyano, dialkylamino, alkylsulfonyl-, alkylsulfonamido-, alkylthio-, carboxyalkyl-, carboxamido-, aminocarbonyl-, optionally substituted aryl and optionally substituted heteroaryl-;

[0019] R_{15} is chosen from optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, and optionally substituted heteroaralkyl-; and

[0020] R_{17} is hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-,

[0021] optionally substituted heteroaryl-, or optionally substituted hetero-aralkyl-, including single stereoisomers, mixtures of stereoisomers;

[0022] a pharmaceutically acceptable salt of a compound of Formula I;

[0023] a pharmaceutically acceptable solvate of a pharmaceutically acceptable solvate of a compound of Formula I; or

[0024] a pharmaceutically acceptable solvate of a pharmaceutically acceptable salt of a compound of Formula I.

[0025] According to one embodiment, when either or R_2 or R_2 , is hydrogen, the other is not hydrogen. In another embodiment, R_2 and R_2 , are each hydrogen; and R_1 is chosen from optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heteroaralkyl, provided however, that R_1 is not substituted phenyl.

[0026] In one aspect, the invention relates to methods for treating cellular proliferative diseases and other disorders that can be treated by inhibiting KSP the administration of a therapeutically effective amount of a compound of Formula I; a pharmaceutically acceptable salt of a compound of Formula I; or a pharmaceutically acceptable solvate of a pharmaceutically acceptable salt of a compound of Formula I, thereof. Such diseases and disorders include cancer, hyperplasia, restenosis, cardiac hypertrophy, immune disorders, fungal disorders and inflammation.

[0027] In another aspect, the invention relates to compounds useful in inhibiting KSP kinesin. The compounds have the structures shown above in Formula I; a pharmaceutically acceptable salt of a compound of Formula I; or a

pharmaceutically acceptable solvate of a pharmaceutically acceptable salt of a compound of Formula I. The invention also relates to pharmaceutical compositions containing a therapeutically effective amount of a compound or Formula I; a pharmaceutically acceptable salt of a compound of Formula I; or a pharmaceutically acceptable solvate of a pharmaceutically acceptable salt of a compound of Formula I, admixed with at least one pharmaceutical excipient. In another aspect, the composition further comprises a chemotherapeutic, agent other than a compound of the present invention.

[0028] In an additional aspect, the present invention provides methods of screening for compounds that will bind to a KSP kinesin, for example compounds that will displace or compete with the binding of a compound of the invention. The methods comprise combining a labeled compound of the invention, a KSP kinesin, and at least one candidate agent and determining the binding of the candidate agent to the KSP kinesin.

[0029] In a further aspect, the invention provides methods of screening for modulators of KSP kinesin activity. The methods comprise combining a compound of the invention, a KSP kinesin, and at least one candidate agent and determining the effect of the candidate agent on the KSP kinesin activity.

BRIEF DESCRIPTION OF THE FIGURES

[0030] The invention will be better understood by reference to the following description taken in conjunction with the accompanying drawings.

[0031] FIGS. 1 and 2 represent a XRPD and MDSC scan, respectively, of a salt prepared according to Preparation A.

[0032] FIG. 3 represents an XRPD scan of a salt prepared according to Preparation B.

DETAILED DESCRIPTION OF THE INVENTION

Definitions

[0033] As used in the present specification, the following words and phrases are generally intended to have the meanings as set forth below, except to the extent that the context in which they are used indicates otherwise. The following abbreviations and terms have the indicated meanings throughout:

- [0034]** Ac=acetyl
- [0035]** Boc=t-butyloxy carbonyl
- [0036]** Bu=butyl
- [0037]** c=cyclo
- [0038]** CBZ=carbobenzoxycarbonyl
- [0039]** DCM=dichloromethane=methylene chloride= CH_2Cl_2
- [0040]** DIEA=N,N-diisopropylethylamine
- [0041]** DMF=N,N-dimethylformamide
- [0042]** DMSO=dimethyl sulfoxide
- [0043]** Et=ethyl
- [0044]** HBTU=O-benzotriazol-1-yl-N,N,N',N'-tetramethyluronium hexafluorophosphate
- [0045]** HMDS=hexamethyldisilazane
- [0046]** HOAc=acetic acid
- [0047]** IPA=isopropyl alcohol
- [0048]** Me=methyl
- [0049]** Ph=phenyl
- [0050]** Py=pyridine
- [0051]** rt=room temperature
- [0052]** sat'd=saturated